
بسم الله الرحمن الرحيم
السلام عليكم ورحمة الله وبركاته



Armed Forces College of Medicine

AFCM



Analgesic Antipyretics

(2)

Professor Dr/ Omayma Khorshid

INTENDED LEARNING OBJECTIVES (ILO)

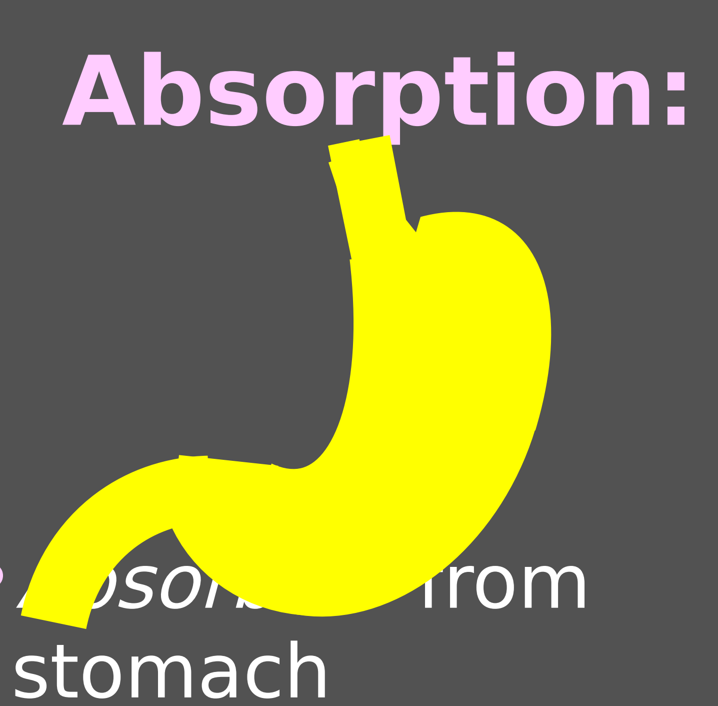
By the end of this lecture the student will be able to:

1. Relate the pharmacokinetic properties of aspirin to its clinical uses ,adverse effects and drug – drug interactions
2. Explain the adverse effects ,drug – drug interactions and contraindications of aspirin

Salicylates

Pharmacokinetics:

Absorption:



- *Absorbed* from stomach
- *But More & complete* absorption from intestine (More surface area).

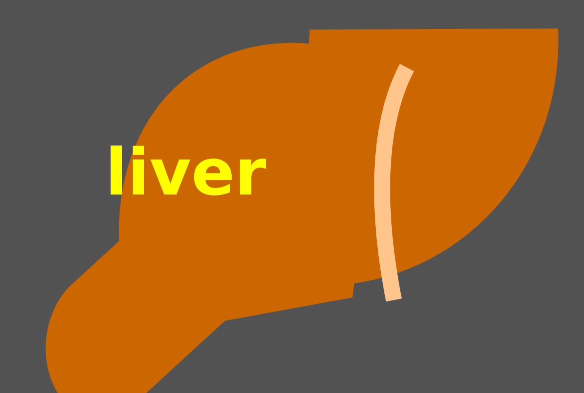
Distribution:



- Highly bound to p.proteins
- Displaces other drugs

Salicylates Pharmacokinetics:

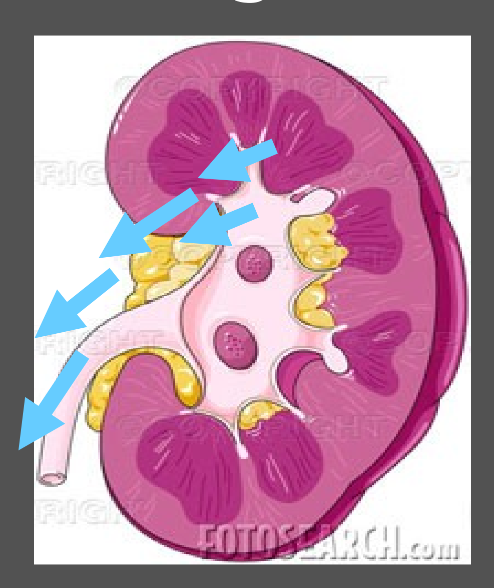
Metabolism:



- Mostly conjugated

Excretion:

Partially Excreted unchanged in urin



Alkalinization of urine



Salicylates

Pharmacokinetics:

Low dose $< 2 gm/day \rightarrow$ First Order Kinetics

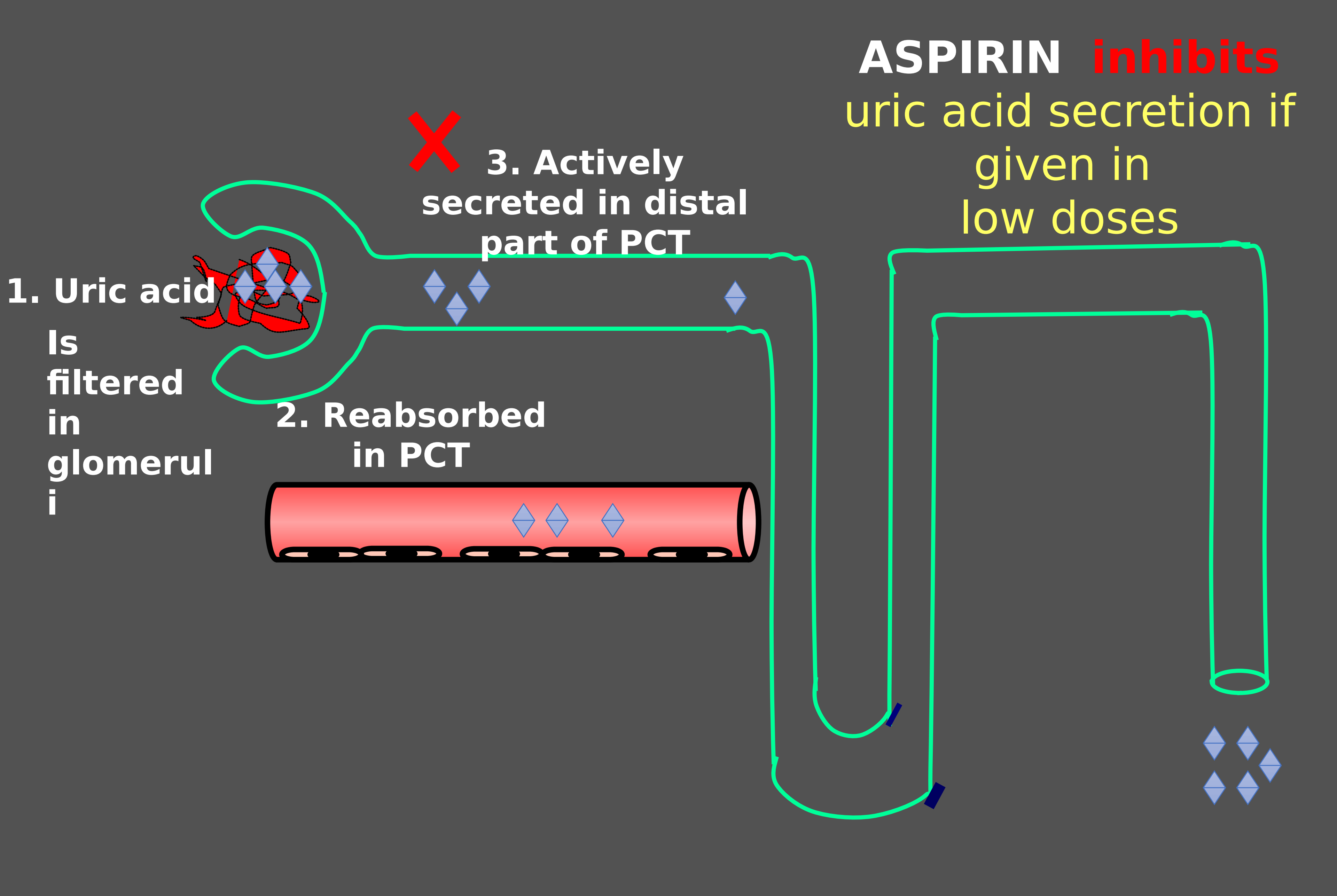
High dose $> 4\ gm/day \rightarrow$ Zero Order Kinetics

pirin is an organic acid & secreted in uri

□ it affect uric acid secretion in urine :

low doses ↓ uric acid secretion □ **# # in gout**

high doses □ no effect or ↑ uric acid secretion


ASPIRIN inhibits
uric acid secretion if
given in
low doses
X
3. Actively
secreted in distal
part of PCT
1. Uric acid
Is
filtered
in
glomerul
i
2. Reabsorbed
in PCT

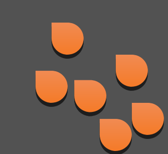
Side Effects

1- Gastric irritation:



- **Peptic ulcer**
- **Bleeding**

2- Bleeding Tendency (↓ platelet aggregation)

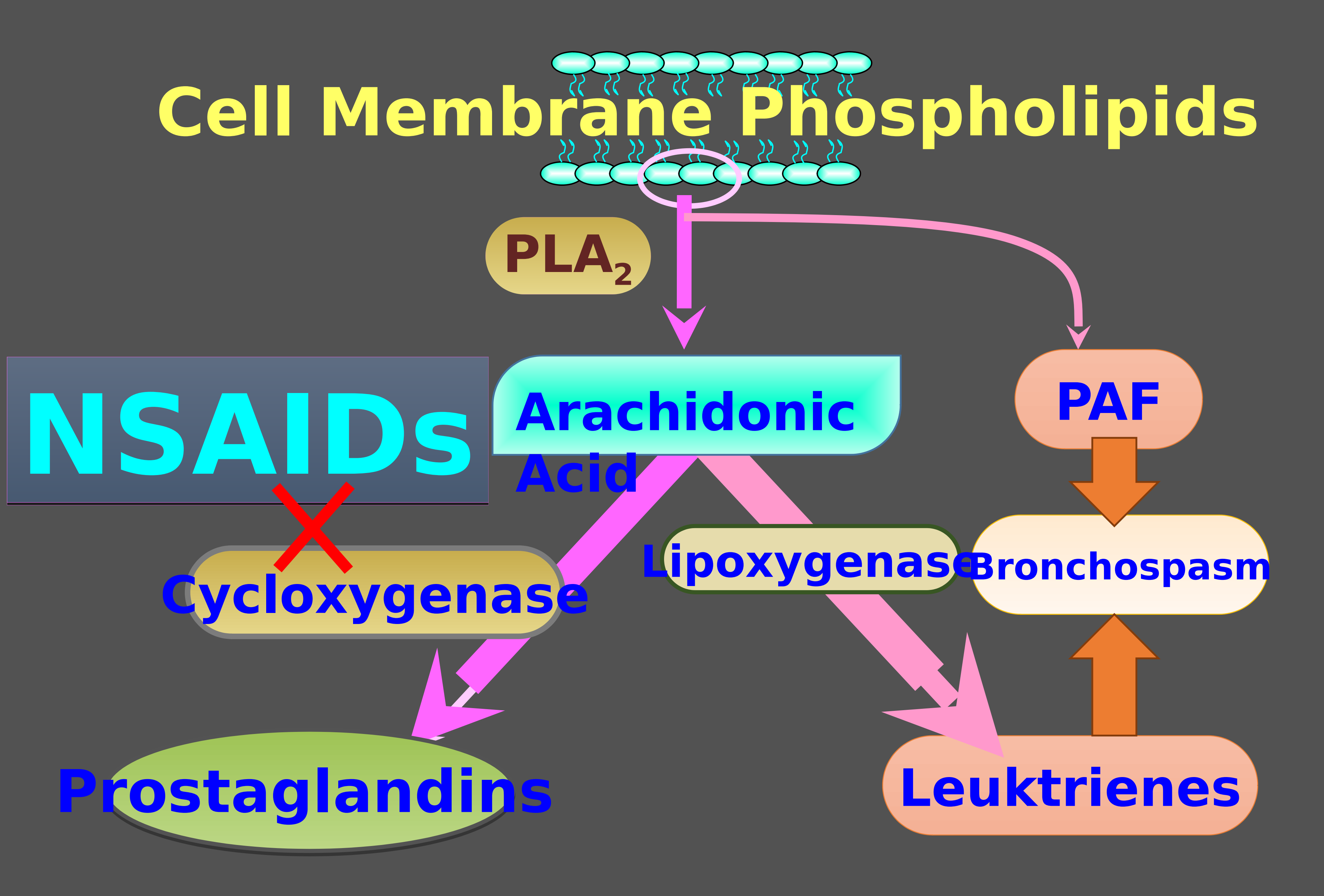


3- Nephropathy



4- Aspirin-induced asthma :

Bronchial asthma in predisposed pat


Cell Membrane Phospholipids
PLA2
Arachidonic Acid
PAF
NSAIDs
Lipoxygenase
Bronchospasm
Cycloxygenase
Prostaglandins
Leuktrienes

Side Effects

5- Reye's syndrome:

- Rare syndrome occurs if aspirin is given to **children with viral infection**

Don't give aspirin in < 20 years

- It consists of:

Fatal hepatotoxicity

Encephalopathy



Reye's syndrome was recorded to occur with the use of which of the following drugs?

a) Aspirin.
b) Diclofenac.
c) Ibuprofen.
d) Paracetamol.
e) Indomethacin.

Side Effects

6- Idiosyncrasy:

Hemolysis in patients with G6PD deficiency (Favism).

7- Allergy:





- Rash & Urticaria
- Angio-edema

8- Teratogenicity: **in pregnancy (risk category C)**

esp. in the 3rd trimesters avoid NSAIDs due to the

Side Effects

➢ Acute Toxicity (severe):

- Salicylates have a high therapeutic index.
- Toxic dose > 200 mg / kg.

Manifestations:

- Restlessness, convulsions,
- Hyperpyrexia (due to uncoupling of oxidative phosphorylation)
- Respiratory and metabolic acidosis
- Coma and death from respiratory failure

Acute Toxicity

No specific antidote

- **Management:**
  - Gastric lavage with $NaHCO_3$
  - Alkalinization of urine (↑ excretion of salicylate).

    Haemodialysis in severe cases
  - Cold fomentation for hyperpyrexia.
  - Correction of dehydration and acid/base imbalance.
  - Vit K & Fresh blood transfusion.
  - Anti-convulsants.

- **Mild toxicity : Salicylism**
  - Occurs after repeated administration of large doses as in treatment of gout or Rh fever.
- **Manifestations:**
  - Tinnitus, blurring of vision, irritability, hyperventilation, & GIT upset.
- **Symptoms are** Reversible after stoppage of treatment.

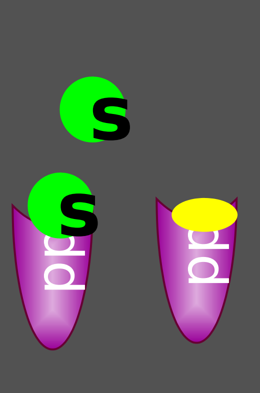
Salicylates – Contraindications

- Gastritis or peptic ulcer
- Bleeding Tendency
- Bronchial asthma
- In children with viral infection (Influenza or Chicken pox)
- Renal diseases
- Favism
- Allergy

Salicylates

Drug Interactions:

- **Salicylates displaces other drugs from plasma proteins e.g:**



Oral anticoagulants
Oral hypoglycemics
Phenytoin & valporic acid

Which of the following mechanisms explain the increase in the risk of bleeding if Aspirin is administered with warfarin ?

a) Aspirin increases absorption of warfarin .

b) Aspirin inhibits the metabolism of warfarin
c) Aspirin displaces warfarin from plasma protein
d) Aspirin inhibits the excretion of warfarin
e) Aspirin inhibits coagulation factors synthesis





Summary

- Aspirin in:
  Low dose < 2gm/day → First Order Kinetics
  High dose > 4 gm/day → Zero Order Kinetics

  Low doses decrease uric acid secretion →**NOT** used in gout
  High doses → no effect or increase uric acid secretion

- Side effects of aspirin:
  Most important is: Peptic ulcer, bleeding tendency, aspirin-induced asthma, reye's syndrome and hemolysis in favism.

- Salicylates displaces other drugs from plasma proteins like:
  Oral anticoagulants, Oral hypoglycemics, phenytoin & valporic acid → increase its cocentration → increase their toxicity

SUGGESTED TEXTBOOKS



1. Whalen, K., Finkel, R., & Panavelil, T. A. (2018) Lippincott's Illustrated Reviews: Pharmacology (7th edition.). Philadelphia: Wolters Kluwer

2. Katzung BG, Trevor AJ. (2018). Basic & Clinical Pharmacology (14th edition) New York: McGraw-Hill Medical.

Thank You